REMARKS

Claims 19, 25, 32 and 38 have been cancelled.

Claims 21, 26-27, 34, 39-40 and 45 have been amended. Support for the amendments can be found throughout the specification, but in particular at paragraphs [0014]; [0027] and Figure 3 of the published application; and the Sequence Listing at SEQ ID NO:1, (ix) feature location 121-122 for the FIN-Major mutation. No new matter has been added by these amendments.

Rejection of Claims 19, 21-25, 27-32, 34-38, 40-45 and 47-48 Under 35 U.S.C. § 112, First Paragraph

Claims 19, 21-25, 27-32, 34-38, 40-45 and 47-48 are rejected under 35 U.S.C. § 112, First Paragraph as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The Examiner believes that the specification teaches a single NPHS1 sequence as well as only two examples of mutations of the Nephrin protein and that there is insufficient written description for the variants of the gene as claimed.

The Examiner believes that the claims recite a genus of sequences containing mutations and that under current PTO Written Description Guidelines, the representative number of species is insufficient to support the genus claims. In particular, the Examiner states that the claims encompass a genus of NPHS1 proteins or nucleic acids which are different that those disclosed in the specification. "In particular, the specification teaches a single NPHS1 sequence, SEQ ID NO: 1, as well as two examples of mutations of the Nephrin sequence, a deletion of 2 base pairs and a nonsense mutation. However, the claimed genus includes variants for which no written description is provided in the specification."

The Examiner goes on to state that: "In a gene that is over 4000 nucleotides in length, there are 3^{4000} (or about $3X10^{1908}$) possible single point mutations alone, not including the other types of mutations. Thus, applicant has express possession of only

two particular mutations of NPHS1 in a genus which comprises hundreds of millions of different possibilities." (Pages 3-4 of the Office Action)

The Examiner cites the CAFC decision, The Regents of the University of California v. Eli Lilly and Co, 43 USPQ2d 1398 (Fed. Cir. 1997) "...[N]aming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." The Examiner states: "In the current situation, the definition of NPHS1 in the claims completely lacks any specific structure, and represents precisely the situation of naming a type of material which is generally known to likely exist, but, except for the two specific variants, is in the absences of knowledge of the material composition and fails to provide descriptive support for the generic claim to a 'NPHS1 gene', for example.

Applicants respectfully disagree. The Claims specifically recite that the methods of detecting basement membrane disease, and in particular congenital nephritic syndrome of the Finnish Type, comprise detecting the one or two mutations in the NPHS1 gene comprising SEQ ID NO: 1 that the Examiner specifically states are described in the specification. Applicants request clarification as to why the Examiner believes that these claims are insufficiently supported by the description in the application.

The Written Description Guidelines state that the written description requirement for a claimed genus may be satisfied by description of a sufficient number of representative species, and that this requirement can be satisfied by functional characteristics coupled with a known or disclosed correlation between function and structure. The purpose of sufficient written description is to reasonably convey to one skilled in the relevant art that the inventors, at the time of the invention, had possession of the claimed invention. The claimed invention encompasses methods of detecting a disease in a subject by detecting mutations in the NPHS1 gene, or detecting additional mutations in the gene. One of skill in the art is a professional (e.g., a physician) familiar with diagnosing genetic diseases. The structure of the NPHS1 gene is known (SEQ ID NO:1) and its function is to code an active nephrin protein. If there is a mutation in the gene structure so that an active protein is not encoded, function is disrupted. Those of skill in the art will determine whether a subject exhibits symptoms of a basement

membrane disease such as congenital nephrotic syndrome of the Finnish Type. The physician will then order the diagnostic assay and determine whether the subject's nucleotide sequence of the NPHS1 gene differs from a control sequence. If the sequence differs from the control, the physician makes the diagnosis. There are two major mutations detected so far, but there may be others that are also associated with the disease. It is important to remember that the "heart" of applicants' invention is the NPHS1 gene as discovered by applicants and association of mutations in the gene with disease. Prior to applicants' discovery of the NPHS1 gene, no cause for the disease had been known. To limit applicants' invention to merely two mutations that were used as prototype examples in the application would be to eviscerate the claimed invention.

These claims all comply with the Written Description requirement as discussed in the very recent CAFC decision Capon v. Eshhar, 76 U.S.P.Q.2d 1078 (Fed. Cir., August 12, 2005). In brief, the CAFC decided that the Written Description requirement of 35 U.S.C. §112, first paragraph, does not impose a per se rule requiring a nucleotide-by-nucleotide re-analysis when the structure of the component DNA segments is already known, or readily determined by known procedures. The court reiterated that the descriptive text needed to meet the Written Description requirements varied from case to case with the nature and scope of the invention and with the state of the scientific and technological knowledge already in existence. In this case, the structure of the gene is known and the methods claimed determine differences in nucleic acids contained in a sample obtained from a subject and the nucleic acid sequence SEQ ID NO: 1. "It is not necessary that every permutation within a generally operable invention be effective in order for an inventor to obtain a generic claim, provided that the effect is sufficiently demonstrated to characterize a generic invention" (Capon v. Eshhar, 76 U.S.P.Q.2d 1078) (Fed. Cir. 2005).

Applicants describe specific examples of mutations of the NPHS1 gene, but also have described the methods to detect additional mutations. It is clear that Applicants' were in possession of the invention as claimed and thus fulfill the written description requirements of 35 U.S.C § 112, first paragraph. However, solely wishing to speed prosecution, Applicants' have cancelled Claims 19, 25, 32 and 38 and have amended

Claims 21, 26, 34, 39 and 45. Claims 22-24, 27-31, 35-37, 40-44 and 47-48 dependent from Claims 21, 26, 34, 39 and 45 and carry the same limitations as the claims from which they depend. The amended claims recite only the two mutations recognized by the Examiner and thus moot the written description rejection.

Rejection of Claims 19, 21-32, 34-45, 47-49 and 51-53 Under 35 U.S.C. § 102(a)

Claims 19, 21-32, 34-45, 47-49 and 51-53 are rejected under 35 U.S.C. § 102(a) as being anticipated by Kestila et al (Mol. Cell 1:575-582 (March 1998)).

The instant application referred to herein as the '622 application, is a divisional application of USSN 09/040,774 now US Patent No. 6,207,811 and referred to herein as the '811 patent. The '622 application is entitled to the March 18, 1998 priority date of the '811 patent. Attached herein is the Exhibit which is a copy of a communication from the publisher of the journal, Molecular Cell, stating that the Kestila et al. paper was published online on March 19, 1998 and the print version of the paper became available on March 20, 1998. Thus, the Kestila et al paper is not prior art to the instant application and withdrawal of the rejection is respectfully requested.

CONCLUSION

The claims are now in condition for allowance. Applicants respectfully request reconsideration and withdrawal of the rejections. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned.

Respectfully submitted,

HAMILTON, BROOK, SMITH &
REYNOLDS, P.C.

By Doreen M. Hogle
Doreen M. Hogle
Registration No. 36,361
Telephone: (978) 341-0036
Facsimile: (978) 341-0136

Concord, MA 01742-9133
Dated: April 20, 2006

Doreen Hogle

From: Doreen Hogle
Sent: Friday, April 14, 2006 4:27 PM
To: Doreen Hogle
Subject: FW: publication date information 0856.2038-001

-----Original Message-----
From: [redacted]
Sent: Thursday, March 09, 2006 4:35 PM
To: [redacted]
Subject: RE: publication date information

Dear Ms. [redacted]

The online publication for this issue was noon on March 19, 1998. The print journal was available on the following day, March 20, 1998.

Best wishes,

[redacted]

[redacted]
Cell Press
600 Technology Square, 5th Floor
Cambridge, MA 02139
ph: 617 397 2859
fax: 617 397 2820

From: [redacted]
Sent: Thursday, March 09, 2006 4:27 PM
To: molecule@cell.com; [redacted]
Subject: publication date information

Dear Persons,

I need to determine the exact publication date of Molecular Cell, Volume 1, issue 4, with a cover date of March 1998. This would be the date on which the journal was mailed to subscribers. Can you provide me with that information, please? Thank you for your help.

[redacted]

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anne.stein@hbsr.com